Spontaneous remission of congenital AML with skin involvement and t(1;11)(p32;q23)

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AML	Acute Myeloid Leukemia
TMD	Transient Myeloproliferative Disorder
BPDCN	Blastic Plasmacytoid Dendritic Cell Neoplasm
ALL	Acute Lymphoblastic Leukemia
DS	Down Syndrome

Congenital/infant acute myeloid leukemia (AML) has poor outcome despite aggressive therapy with rare instances of spontaneous remission. The two well-known entities with spontaneous remission are transient myeloproliferative disorder (TMD) seen in Down syndrome (DS) newborns and infant AML with t(8;16)(p11;p13). While most TMD cases resolve spontaneously, 20-30% would present with AML later. [1] Leukemia cutis is common in spontaneously regressing infant AML with t(8;16)(p11;p13); among 7 infants reported, 4 relapsed with a median of 17 months.[2-4] Here we report a congenital AML case with t(1;11)(p32;q23) involving the MLL gene with sustained spontaneous remission.

A 2-month old female with an uneventful prenatal history presented with skin lesions first seen at 1-month of age (Figure 1A). There were fading skin lesions, otherwise physical exam was unremarkable. Complete blood count (CBC) and LDH were within normal limits. Skin biopsy revealed CD4 and CD56-positive and myeloperoxidase-negative infiltrating monotonous cells with irregular folded and indented nuclei. Bone marrow morphology and flow cytometry findings were consistent with AML (Figure 1B and 1C). Cytogenetic study revealed t(1;11)(p32;q23); FISH analysis showed MLL gene rearrangement, which was negative in the peripheral blood. Cerebrospinal fluid analysis was negative for leukemia cells. Positron emission tomography did not indicate extramedullary site involvement. Peripheral blood natural killer lymphocytes were higher than age-normal range.

Due to already regressing skin lesions, normal CBC, absence of clinical findings and unusual flow cytometric findings and following discussions with her parents, a decision for close monitoring was made. She achieved remission by morphology, cytogenetic and flow cytometric studies in six weeks (Figure1D). Her skin lesions completely resolved and natural killer lymphocytes decreased to normal range. She continues to be in complete remission two years from diagnosis.

Eight percent of congenital AML many with monocytic phenotype undergo spontaneous complete remission. [4] While AML with the t(1;11)(q21;q23) has 100% overall survival rate in childhood, the prognosis of t(1;11)(p32;q23) AML was dismal with a median survival of 15 months. Thirty eight percent of reported leukemia patients with t(1;11)(p32;q23) were infants equally distributed between acute lymphoblastic leukemia (ALL) and AML.[5,6] This translocation was also seen in monozygotic twins with ALL and therapy-related ALL.[7,8] No cases of spontaneously resolving leukemia with t(1;11)(p32;q23) have been reported.

Leukemia cutis is noted frequently at the onset of disease; rare cases preceding diagnosis were reported, likely at the aleukemic phase.[9,10] Skin involvement was reported in congenital AML with t(1;11)(p32;q23).[11] In our case, initial bone marrow involvement pattern was reminiscent of a metastatic disease; whether leukemic process started in the skin remains unknown. Leukemia cell maturation at diagnosis points at in utero initiation of the process.

Our patient with unique features of leukemia cutis, normal CBC, bone marrow infiltration pattern, lack of CD45-dim clonal cells with maturation in abnormal cells, presence of t(1;11)(p32;q23) with MLL gene rearrangement and the achievement of sustained spontaneous remission raises the possibility of similar cases achieving spontaneous remission that might go unrecognized, with or without resurgence of AML. Further molecular analysis would potentially shed light on the mechanism of spontaneous remission in this otherwise high-risk AML type.

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Conflict of interest statement:

The authors do not have any relevant conflict of interest to declare.

Figure Legend: 1A. Raised skin lesions were red/purple in color and spread over time, then started to fade slowly leaving mild hyperpigmentation behind. 1B. Bone marrow aspiration showed patchy infiltration with immature large cells making up to 12% of the cellularity, despite overall well-preserved tri-lineage hematopoiesis with increased megakaryocytes and absent dysplastic changes. Abnormal cells had bean-shaped and folded nuclei and 2-3 nucleoli resembling immature monocytic cells accompanied by several mitotic and apoptotic figures. In addition to the occasional immature cells among the normal marrow elements, there were sheets of immature monocytic cells on the aspirate constituting as high as 85% of cellularity in the respective areas. 1C. Flow cytometric analysis did not reveal a distinct CD45-dim/negative clonal leukemia population on side scatter/CD45 histogram; however, gating on the wider monocyte population showed a subpopulation of immature cells that were largely myeloperoxidase-negative, similar to what was observed in the leukemia cells that infiltrated the skin. Abnormal monocytic cells expressed CD4 and partial CD14 and CD56, but were largely negative for CD123. 1D. Six weeks from her presentation, bone marrow flow cytometric study showed maturation of these immature monocytic cells with increasing expression of CD14 and loss of CD56 expression.